

=> d his

(FILE 'HOME' ENTERED AT 11:43:46 ON 15 JAN 2009)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 11:44:21 ON 15 JAN 2009

E EBBEHOJ KIRSTEN /AU
L1 7 S E3
E JEPSEN TRINE /AU
L2 7 S E3
E KNUDSEN CARSTEN /AU
L3 21 S E3-5
E LARSEN BJARNE /AU
L4 76 S E3-5
E KOTT DAVID /AU
E KNOTT DAVID /AU
L5 8 S E3
L6 105 S L1-5
L7 2 S L6 AND EXENDIN?
L8 2 DUP REM L7 (0 DUPLICATES REMOVED)
L9 2135 S EXENDIN?
L10 42 S ASP 28
L11 0 S L10 AND L9
L12 23 S L9 AND ASPARTIC?
L13 1 S L12 AND POSITION

FILE 'HOME' ENTERED AT 16:17:56 ON 13 JAN 2009

=> file registry

FILE 'REGISTRY' ENTERED AT 16:18:39 ON 13 JAN 2009

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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 12 JAN 2009 HIGHEST RN 1093343-19-1
DICTIONARY FILE UPDATES: 12 JAN 2009 HIGHEST RN 1093343-19-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=> S HGEFTFTSDLSKQMEEEEAVRLFIEWLKDGGPSSGAS
L1 0 HGEFTFTSDLSKQMEEEEAVRLFIEWLKDGGPSSGAS

=> S HGEFTFTSDLSKQMEEEEAVRLFIEWLKDGGPSSGAS/SQSP
L2 5 HGEFTFTSDLSKQMEEEEAVRLFIEWLKDGGPSSGAS/SQSP

=> D CN SQL1
'SQL1' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

L2 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2009 ACS on STN
RN 683291-37-4 REGISTRY
ED Entered STN: 19 May 2004

CN L-Lysinamide, L-asparaginyl-L-a-glutamyl-L-a-glutamyl-L-a-glutamyl-L-a-glutamyl-L-a-glutamyl-L-histidylglycyl-L-a-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-a-aspartyl-L-leucyl-L-seryl-L-lysyl-L-glutamyl-L-methionyl-L-a-glutamyl-L-a-glutamyl-L-a-glutamyl-L-alanyl-L-valyl-L-arginyl-L-leucyl-L-phenylalanyl-L-isoleucyl-L-a-glutamyl-L-tryptophyl-L-leucyl-L-lysyl-L-a-aspartylglycylglycyl-L-prolyl-L-seryl-L-serylglycyl-L-alanyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 48

NTE modified

type	-----	location	-----	description
terminal mod.	Lys-48	-		C-terminal amide

SEQ 1 NEEEEHGEFTFTSDLSKQM EEEAVRLFIE WLKDGGPSSG
ASKKKKKK

HITS AT: 7-42

SEQ3 1 Asn-Glu-Glu-Glu-Glu-Glu-His-Gly-Glu-Gly-

11 Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-
 21 Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-
 31 Trp-Leu-Lys-Asp-Gly-Gly-Pro-Ser-Ser-Gly-
 41 Ala-Ser-Lys-Lys-Lys-Lys-Lys-Lys

HITS AT: 7-42

MF Unspecified

CI MAN

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES
 (Uses)

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 140:386038 CA <<LOGINID::20090113>>

TITLE: Stabilized exendin-4 compounds, their preparation, and
 their therapeutic use

INVENTOR(S): Ebbehoj, Kirsten; Jepsen, Trine; Knudsen, Carsten
 Boye; Larsen, Bjarne Due; Knott, David

PATENT ASSIGNEE(S): Zealand Pharma A/S, Den.

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: C07K014-575

CLASSIFICATION: 1-10 (Pharmacology)

Section cross-reference(s): 34, 63

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004035623	A2	20040429	WO 2003-DK651	20031002
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WO 2004035623	A3	20040603		
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2500295 A1 20040429 CA 2003-2500295 20031002
 AU 2003268621 A1 20040504 AU 2003-268621 20031002
 EP 1546200 A2 20050629 EP 2003-747852 20031002
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003014996 A 20050809 BR 2003-14996 20031002
 JP 2006517908 T 20060803 JP 2004-543971 20031002
 NO 2005001585 A 20050620 NO 2005-1585 20050329
 MX 2005PA03335 A 20050705 MX 2005-PA3335 20050329
 ZA 2005002571 A 20060222 ZA 2005-2571 20050330
 IN 2005KN00552 A 20060224 IN 2005-KN552 20050401
 US 20060194719 A1 20060831 US 2006-529858 20060426
 PRIORITY APPLN. INFO.: US 2002-415626P 20021002
 WO 2003-DK651 20031002

ABSTRACT:

The invention discloses compns. comprising a stabilized Exendin-4 (1-39) and related compds. The invention describes stabilized Exendin-4 agonists that include at least one modified amino acid residue particularly at positions Gln 13, Met14, Trp25, or Asn28 of the Exendin-4 (1-39) mol. Disclosed are preferred modifications of deaminated, hydrolyzed, oxidized, or isomerized reaction products of the specified amino acid residues corresponding to the same positions in the Exendin-4 mol. The invention also relates to methods of making and using the stabilized Exendin compds., such as for the treatment of diabetes.

SUPPL. TERM: stabilized exendin 4 compd prepn therapeutic; antidiabetic
 stabilized exendin 4 compd

INDEX TERM: Functional groups
 (3H-indol-3-yl, oxidized; stabilized exendin-4 compound
 preparation and therapeutic use)

INDEX TERM: Metals, biological studies
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (and metal ions; stabilized exendin-4 compound preparation and
 therapeutic use)

INDEX TERM: Drug delivery systems
 (depot; stabilized exendin-4 compound preparation and
 therapeutic use)

INDEX TERM: Heart, disease

(infarction; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Autoimmune disease
(insulin-dependent diabetes mellitus; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Diabetes mellitus
(insulin-dependent; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Drug delivery systems
(liposomes; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Drug delivery systems
(liqs.; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Drug delivery systems
(microspheres; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Diabetes mellitus
(non-insulin-dependent; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Solid phase synthesis
(peptide; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Temperature
(room temperature; stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Air
Antidiabetic agents
Antiobesity agents
Cardiovascular agents
Drug delivery systems
Eating disorders
Gastric emptying
Heat
Human
Hyperglycemia
Hypolipemic agents
Light
Metabolic disorders
Obesity
Stability
Stomach, disease
Water vapor
(stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: Hyperlipidemia

ROLE: BSU (Biological study, unclassified); BIOL (Biological

study)
(stabilized exendin-4 compound preparation and therapeutic use)
INDEX TERM: Peptides, biological studies
ROLE: PAC (Pharmacological activity); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(stabilized exendin-4 compound preparation and therapeutic use)
INDEX TERM: 683749-09-9
ROLE: PAC (Pharmacological activity); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(202; stabilized exendin-4 compound preparation and therapeutic
use)
INDEX TERM: 50-99-7, D-Glucose, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(impaired glucose tolerance; stabilized exendin-4 compound
preparation and therapeutic use)
INDEX TERM: 9004-10-8, Insulin, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(insulin resistance syndrome; stabilized exendin-4 compound
preparation and therapeutic use)
INDEX TERM: 56-84-8, L-Aspartic acid, biological studies 56-85-9D,
L-Glutamine, derivs. 63-68-3D, L-Methionine, oxidized
70-47-3D, L-Asparagine, derivs. 73-22-3D, L-Tryptophan,
oxidized 343-65-7, Kynurenine 484-78-6,
3-Hydroxykynurenine 1022-31-7, N-Formylkynurenine
2353-44-8 3226-65-1 5615-80-5, Aspartimide 7314-32-1
7732-18-5, Water, biological studies 7782-44-7, Oxygen,
biological studies 683291-28-3
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(stabilized exendin-4 compound preparation and therapeutic use)
INDEX TERM: 683291-29-4 683291-30-7 683291-31-8 683291-32-9
683291-33-0 683291-34-1 683291-35-2 683291-36-3
683291-37-4 683291-38-5 683749-07-7 683749-08-8
683749-10-2 683749-11-3 683749-18-0D, derivs.
683749-19-1 683749-20-4 683749-21-5 683749-22-6
683749-23-7 683749-24-8 683749-25-9 683749-25-9D,
derivs. 683749-26-0 683749-26-0 683749-27-1
683749-27-1 683749-28-2 683749-29-3 683749-30-6
683749-31-7 683749-32-8 683749-33-9 683749-34-0
683749-35-1 683749-36-2 683749-37-3 683749-38-4
683749-39-5 683749-40-8 683749-41-9 683749-42-0
683749-43-1 683749-44-2 683749-48-6 683749-49-7
683749-49-7D, derivs. 683749-51-1D, derivs. 683749-52-2
683749-53-3 683749-54-4 685505-33-3 685505-35-5D,

derivs. 685505-36-6D, derivs. 685505-37-7D, derivs.
685505-38-8D, derivs. 685505-39-9D, derivs.
685505-40-2D, derivs. 685505-41-3D, derivs.
685505-42-4D, derivs. 685505-43-5D, derivs.
685505-44-6D, derivs. 685505-45-7 685505-46-8
685505-47-9 685505-48-0 685505-49-1 685505-50-4D,
derivs. 685505-51-5D, derivs. 685505-52-6D, derivs.
685505-59-3D, derivs. 685505-83-3D, derivs.
685506-08-5D, derivs. 685506-14-3D, derivs.
685506-15-4D, derivs. 685506-16-5D, derivs.
685506-17-6D, derivs. 685506-18-7D, derivs.
685506-19-8D, derivs. 685506-20-1D, derivs.
685506-21-2D, derivs. 685506-22-3D, derivs. 685506-23-4
685506-24-5

ROLE: PAC (Pharmacological activity); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized exendin-4 compound preparation and therapeutic use)

INDEX TERM: 683291-39-6

ROLE: PRP (Properties)
(unclaimed protein sequence; stabilized exendin-4
comps., their preparation, and their therapeutic use)

INDEX TERM: 684310-50-7 684310-51-8 684310-52-9 684310-53-0
684310-54-1 684310-55-2

ROLE: PRP (Properties)
(unclaimed sequence; stabilized exendin-4 comps., their
preparation, and their therapeutic use)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE
FOR THIS

RECORD.

REFERENCE(S): (1) Anon; WO 0066629 A1 CAPLUS
(2) Anon; WO 0104156 A1 CAPLUS
(3) Anon; DE 19637230 A1 CAPLUS
(4) Anon; WO 9943708 A1 CAPLUS

=> D CN SQL SEQ 2

L2 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2009 ACS on STN
CN L-Lysinamide, L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-
histidylglycyl-L-a-glutamylglycyl-L-threonyl-L-phenylalanyl-L-
threonyl-L-seryl-L-a-aspartyl-L-leucyl-L-seryl-L-lysyl-L-glutaminyl-
L-methionyl-L-a-glutamyl-L-a-glutamyl-L-a-glutamyl-L-
alanyl-L-valyl-L-arginyl-L-leucyl-L-phenylalanyl-L-isoleucyl-L-a-
glutamyl-L-tryptophyl-L-leucyl-L-lysyl-L-a-aspartylglycylglycyl-L-
prolyl-L-seryl-L-serylglycyl-L-alanyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-L-
lysyl-L-lysyl- (9CI) (CA INDEX NAME)

SQL 48

SEQ 1 KKKKKKHGEG TFTSDLSKQM EEEAVRLFIE WLKDGGPSSG
ASKKKKKK

HITS AT: 7-42

=> D CN SQL SEQ 3

L2 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2009 ACS on STN
CN L-Lysinamide, L-histidylglycyl-L-a-glutamylglycyl-L-threonyl-L-
phenylalanyl-L-threonyl-L-seryl-L-a-aspartyl-L-leucyl-L-seryl-L-
lysyl-L-glutaminy-L-methionyl-L-a-glutamyl-L-a-glutamyl-L-
a-glutamyl-L-alanyl-L-valyl-L-arginyl-L-leucyl-L-phenylalanyl-L-
isoleucyl-L-a-glutamyl-L-tryptophyl-L-leucyl-L-lysyl-L-a-
aspartylglycylglycyl-L-prolyl-L-seryl-L-serylglycyl-L-alanyl-L-seryl-L-
lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)

SQL 42

SEQ 1 HGEGTFTSDL SKQMEEEA VR LFIEWLKDGG PSSGASKKKK KK

HITS AT: 1-36

=> FIL MEDLINE CAPLUS BIOSIS

COST IN U.S. DOLLARS

ENTRY	SESSION	TOTAL
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FULL ESTIMATED COST

70.47	70.69
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL

ENTRY	SESSION
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CA SUBSCRIBER PRICE

-0.78	-0.78
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FILE 'CAPLUS' ENTERED AT 16:30:37 ON 13 JAN 2009

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FILE 'BIOSIS' ENTERED AT 16:30:37 ON 13 JAN 2009

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=> S L2

L3 I L2

=> D L3

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:354975 CAPLUS <<LOGINID::20090113>>

DN 140:386038

TI Stabilized exendin-4 compounds, their preparation, and their therapeutic use

IN Ebbehøj, Kirsten; Jepsen, Trine; Knudsen, Carsten Boye; Larsen, Bjarne Due; Knott, David

PA Zealand Pharma A/S, Den.

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004035623	A2	20040429	WO 2003-DK651	20031002
WO 2004035623	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2500295	A1	20040429	CA 2003-2500295	20031002
AU 2003268621	A1	20040504	AU 2003-268621	20031002
EP 1546200	A2	20050629	EP 2003-747852	20031002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014996	A	20050809	BR 2003-14996	20031002
JP 2006517908	T	20060803	JP 2004-543971	20031002
NO 2005001585	A	20050620	NO 2005-1585	20050329
MX 2005PA03335	A	20050705	MX 2005-PA3335	20050329
ZA 2005002571	A	20060222	ZA 2005-2571	20050330
IN 2005KN00552	A	20060224	IN 2005-KN552	20050401
US 20060194719	A1	20060831	US 2006-529858	20060426
PRAI US 2002-415626P	P	20021002		
WO 2003-DK651	W	20031002		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT